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Twelve Year Analysis of Aerobic-Only Blood Cultures for Routine Detection of Bacteraemia.

Simon Stoneham^{1,2,3}, William Schilling¹, Alberto San Francisco ¹, Martin Llewelyn^{1,2}

1. Department of Microbiology and Infection, Royal Sussex County Hospital, Brighton, UK

2. Department of Global Health and Infection, Brighton and Sussex Medical School, Falmer, UK

3. Corresponding author. Department of Microbiology and Infection, Royal Sussex County Hospital, Brighton, UK. Tel: 07950401183 Email: simon.stoneham@nhs.net

Keywords

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Sampling practice

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Summary

Sampling practices determine the accuracy of blood culture in diagnosing bloodstream infection. Our main acute hospital introduced aerobic-only routine blood cultures aiming to increase the volume and number of aerobic samples. At a smaller acute site aerobic-anaerobic pairs were sent routinely. We compared culture yield and sampling practices at these two sites and found anaerobic cultures increased the yield of pathogens including facultative anaerobes. Volume cultured and number of samples sent fell short of national recommendations. The aerobic-only policy did not result in more blood being cultured. based on these findings we are reintroducing aerobic-anaerobic pairs for routine culture.

Introduction

Blood cultures provide vital information for patient management and remain the mainstay of diagnosis in bacteraemic patients. However, sample handling impacts on both sensitivity and specificity of cultures. Recommendations in the UK (Standards for Microbiological Investigation) and internationally are that at least two sets of paired aerobic and anaerobic samples, taken within 24 hours, be sent for culture in most situations with a volume of 20-30 mL per set [1, 2]. Use of single aerobic bottle sets is only supported in the instance of low volume of blood obtained [1]. These recommendations are based on evidence that low volume cultures have both reduced sensitivity and a higher contamination rate [3]. Taking multiple cultures assists in determining when likely contaminants, such as coagulase-negative staphylococci, are in fact present in blood as pathogens [4]. Although the volume of blood inoculated is a major factor in determining the sensitivity of blood culture, in reality, most blood cultures sent have inadequate volumes and are sent as single sets [5]. Vacuum-based blood culture systems have a standard fill volume to achieve an optimal blood-to-broth ratio, making over-filling difficult to achieve, as this may decrease sensitivity [6]. Increasing the number of bottles inoculated is a valid strategy for increasing the volume of blood sampled and therefore increase the detection of bacteraemia [1].

The value of routine anaerobic cultures has been challenged on the basis that the rates of fastidious and anaerobic bacteraemia are falling, whereas rates of candidal and aerobic bacteraemia have increased [7].

At our hospital Trust a decision was made 12 years ago to switch to routine single aerobic bottle only blood cultures at the main acute hospital site, with the aim of increasing the proportion of patients in whom 2 cultures were performed and increase the blood volume inoculated per bottle. At the Trust's smaller acute site policy remained to take blood culture sets comprising aerobic-anaerobic pairs.

Methods

Setting

Brighton and Sussex University Hospitals NHS Trust includes two acute sites: The Royal Sussex County Hospital (RSCH) in Brighton (approx. 600 beds) and the Princess Royal Hospital (PRH) in Haywards Heath (approx. 300 beds). Both sites have an Emergency Department and Acute Medical Unit receiving emergency admissions. BD Bactec Standard bottles are used at both sites and processed at a central lab based at RSCH where samples are loaded onto an BD Bactec FX automated blood culture analyser.

Blood culture data

Records of all blood cultures received from adult (≥ 18 years) patients between 15/10/2006 to 30/04/2018. were obtained from the Laboratory Information Management System (WinPath). Data were gathered on patient location, culture results and time to positivity.

Definitions

Where multiple names were used for the same organism synonyms were grouped together e.g. *Streptococcus pyogenes* and group A streptococcus. The analysis of *Staphylococcus aureus* included Methicillin Resistant *Staphylococcus aureus*. All coagulase negative staphylococci that were identified to the species level were grouped together as coagulase negative staphylococci. Anaerobes only included organisms identified to this level and did not include organisms with a specific species identification. Sets were classified as 'other' if they contained an organism not otherwise categorised and did not contain an organism from another category.

Given the policy to take only aerobic bottles the term 'set' refers to either an aerobic-anaerobic bottle pair or a single aerobic bottle if that was the only sample received.

To assess the number of blood culture sets taken per episode of infection we considered sets received on the same day to have been taken for the same episode.

Volume of cultured blood

To assess volumes of blood being taken for culture, all blood culture bottles were weighed for a 10 day period (7th-17th July 2018) at the end of incubation (n=678). Mean bottle weights were obtained by weighing 16 consecutive empty aerobic and anaerobic bottles respectively.

Statistics

Data analysis was performed using Microsoft Excel and SPSS. Where appropriate Z-tests were used to compare independent proportions and t-tests were used to compare independent means.

Ethics

According the NHS Health Research Authority definitions this work was a service evaluation using only routinely gathered patient data and not requiring ethics review [8].

Results and Discussion

During the period studied, 151 278 blood cultures were processed in the laboratory, 122 939 (81%) from the RSCH site (32 870 [27% aerobic-anaerobic pairs]) and 28 339 (19%) from the PRH site (24 402 [86% aerobic-anaerobic pairs]). These equate to approximately 61.8 and 29.5 cultures performed per 1000 hospital bed days. Data from Public Health England (PHE) indicates the Mean and IQR for acute trusts in the UK is 61.6 and 25.3 respectively [9]. The overall positivity rate was significantly higher at PRH than RSCH (3867/28 339, [13.6%] vs 117/122 939 [10.7%] $P<0.001$). It is impossible to know to what extent these differences are explained by differences in case mix (patients from whom samples were received at PRH were older (64 [IQR 31] vs 62 [IQR 31]), more likely to be female (48% vs 45%) and more likely to be in the emergency department (41% vs 40%) or differences in sampling strategy across sites, although many staff work across both sites where training and policy are aligned.

Among 3448 positive aerobic-anaerobic sets processed from PRH, growth was detected only in the anaerobic bottle in 723 (21%) [Table I]. In keeping with previous studies [10], we find numerous instances where growth was only detected in anaerobic culture for all the key pathogens perhaps unsurprising as many common blood culture isolates are facultative anaerobes. For *S. aureus* and *E. coli*, 16% and 17.2% respectively of cultures only detected growth in the anaerobic bottle. It is nevertheless striking that the rates of identification for each key pathogen are broadly similar comparing paired cultures at PRH with single-aerobic 'sets' taken at the RSCH site. This implies differences in case mix are likely to be small. The rate of identification of *Bacteroides fragilis* is markedly lower at RSCH, unsurprisingly given it is a strict anaerobe.

To assess the relative sensitivity of aerobic and anaerobic cultures for key pathogens, we compared detection rates between aerobic and anaerobic bottles from aerobic-anaerobic pairs taken at PRH, where at least one bottle was positive. We found significantly higher detection rates for *S. aureus* in anaerobic bottles (91.4% vs 82.8% $P=0.006$) and equivalent detection of *E. coli* (84.8% vs 84.4% $P=0.37$) which comprise 25.7% of all positive cultures. Overall, we found that time to positivity (TTP) was longer for anaerobic bottles vs aerobic bottles (25.2Hrs vs 19.9Hrs $P=0.005$) [Table II].

The original rationale for switching to a single aerobic bottle for routine blood culture was that the quality of blood culture sampling would improve by inoculating the same volume of blood from aerobic-anaerobic pairs into single aerobic bottles. This would also allow for a second 'set' to be taken without increasing incubator occupancy. For the most recent full calendar year (2017) we determined the number of patients who had two or more blood cultures sent on the same calendar day. Overall 824/7824 (10.5%) of sampled patients had two or more sets of cultures sent. There was no significant difference between the two hospital sites: 198 / 2029 (9.8%) at PRH and 626 / 5795 (10.8%) at RSCH (P=0.17). This is at odds with recommendations that two or more sets be sent [1,2]. We are not aware of comparable UK data but US rates of single blood culture sets are estimated to be only around 20% [5]. We have no reason to believe that the low rate of repeat sampling in our hospital is exceptional in the NHS but removing anaerobic culture from routine use has clearly not increased the number of repeat culture sets in our practice.

To determine bottle filling, 678 consecutive blood culture samples were weighed at the time of removal from the incubator. Using unfilled bottle weights of 145.5g for aerobic and 146.1g for anaerobic and an average blood density of 1060 Kg/m² we estimated there was no difference between aerobic bottle filling at the two sites (PRH [n = 95] 6.6mL [95% CI 5.7 – 7.4] vs RSCH [n = 362] 6.7mL [95% CI 6.3 – 7.2] P=0.719). Even accounting for the fact that anaerobic bottles from PRH (n = 55) contained less blood compared to RSCH (n=166) (4.7mL [95% CI 3.9—5.6] vs 6.8mL [95% CI 6.2—7.4] P= 0.001). The overall average blood volume per sampling episode was 6.8 mL for single aerobic bottle sets taken at RSCH and 11.3mL for paired aerobic-anaerobic sets taken at PRH. These volumes are considerably below the 40ml draw for blood culture which is widely recommended [1,2,5] on the basis that this achieves sensitivity approaching 90%. Again, we have no reason to believe that the low volumes of blood being taken in our hospital are exceptional in the NHS but removing anaerobic culture from routine use has not led to better bottle filling and has reduced the overall volume being taken.

In conclusion we confirm previous observations that pairing anaerobic with aerobic blood cultures adds usefully to the overall yield of blood culture. We have identified several shortfalls in practice, compared to UK standards, around sampling at our hospital, which we are reporting as we believe it is likely to be typical of acute hospitals in England and probably

elsewhere. We would like to see national assurance initiatives to improve the quality of blood culture practice cover sampling in addition to subsequent handling and analysis. Ahead of this we are reintroducing paired aerobic-anaerobic cultures into routine practice throughout our Trust and establishing ongoing quality improvement work to raise the quality of practice in this area.

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Conflict of Interest

No conflicts of interest were identified.

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Organism	From Aerobic and Anaerobic Bottles in Paired Cultures PRH					From Single Aerobic Cultures RSCH		Difference in Detection Rate [95%CI]
	Aerobic only	Anaerobic only	Both	Total positive	Percentage of Positive	Total Positive	Percentage of Positive	
<i>E. coli</i>	96 (15.2%)	101 (16.0%)	434 (68.8%)	631 (2.59%)	18.5%	1639(1.9%)	17.0%	0.66% [0.45-0.89] P<0.001
<i>S. aureus</i>	22 (8.59%)	44 (17.2%)	190 (74.2%)	256 (1.05%)	7.42%	758(0.89%)	7.86%	0.16% [0.02 – 0.30] P= 0.03
<i>K. pneumoniae</i>	18 (17.8%)	9 (8.91%)	74 (73.3%)	101 (0.41%)	2.93%	309(0.36%)	3.2%	0.08% [-0.04 – 0.14] P=0.20
<i>S. pneumoniae</i>	19 (19.6%)	4 (4.12%)	74 (76.3%)	97 (0.40)	2.81%	281(0.33%)	2.91%	0.07% [-0.02 – 0.15] P=0.11
<i>S. pyogenes</i>	4 (15.4%)	3 (11.5%)	19 (73.1%)	26 (0.11%)	0.75%	104(0.12%)	1.08%	0.001% [-0.06-0.03] P=0.33
<i>Bacteroides fragilis or Anaerobes</i>	0 (0%)	26 (61.9%)	16 (38.1%)	42 (0.17%)	1.22%	12 (0.014%)	0.12%	0.16% [0.11 – 0.21] P<0.001
<i>Coagulase Negative Staphylococci</i>	547 (38.3%)	279 (19.5%)	604 (42.2%)	1430 (5.86%)	41.5%	4003 (4.7%)	41.5%	1.17% [0.85 – 1.50] P<0.001
<i>Other</i>	303 (35.0%)	257 (29.7%)	305 (35.3%)	865 (3.54%)	25.1%	2539 (2.97%)	26.3%	0.57% [0.31-0.83] P<0.001
<i>Total</i>	1009 (29.3%)	723 (21.0%)	1716 (49.8%)	3448/24402 (14.1%)	NA	9645/85398 (11.3%)	NA	2.84% [2.35 – 3.32] P<0.001

Table I: Detection rates for key pathogens between Aerobic-Anaerobic pairs at PRH and single aerobic bottles at RSCH. P-values are derived from Z-tests for independent proportions.

Organism	O2 Detection rate	AnO2 Detection rate	Difference [95%CI]	Mean O2 TTP [SD]	Mean AnO2 TTP [SD]	P- value [TTP]
<i>E. coli</i>	529 (84.0%)	534 (84.8%)	0.79% [-3.21- 4.80] P=0.37	13.2 [14.7]	15.1 [19.2]	0.992
<i>S. aureus</i>	212(82.8%)	234 (91.4%)	8.59% [2.84-14.35] P=0.006	16.6 [14.6]	24.4 [21.8]	<0.001
<i>K. pneumoniae</i>	92 (91.1%)	83 (82.2%)	-8.91% [-18.4-0.55] P=0.07	17.8 [21.8]	16.0 [18.9]	0.525
<i>S. pneumoniae</i>	93 (95.9%)	78 (80.4%)	-15.5% [-24.3 - -6.59] P=0.002	10.8 [10.0]	10.3 [3.29]	0.367
<i>S. pyogenes</i>	23 (88.4%)	22 (84.6%)	-3.85% [-22.9 – 15.2] P=0.37	7.78 [3.12]	8.27 [8.77]	0.272
<i>Bacteroides fragalis</i> or <i>Anaerobes</i>	16 (38.0%)	42 (100%)	61.9% [38.1 – 85.7] P< 0.001	31.3 [37.9]	35.5 [27.6]	0.140
<i>Coagulase Negative Staphylococci</i>	1151 (81.0%)	883(62.2%)	-18.7% [-22.1 - -15.3] P <0.001	21.2 [13.2]	26.4 [18.9]	<0.001
<i>Overall</i>	2725 (78.6%)	2439 (70.3%)	-8.25% [-10.4 - -6.08] P <0.001	19.9 [17.2]	25.2 [26.1]	0.005

Table II: Detection rates and Time To Positivity (TTP) for key pathogens in aerobic-anaerobic paired cultures taken at PRH. For detection rates a Z-test for independent proportions was used and for TTP an independent samples T-test was used.